COMMENTARY

# Cervical Cancer : Is Vaccination Necessary in India?

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## Abstract

**In India, cervical cancer is the most common woman-related cancer, followed by breast cancer. The rate of cervical cancer in India is fourth worldwide. Two vaccines, Gardasil and Cervarix, both targeting HPV-16 and 18 which account for 70% of invasive cervical carcinomas, are licensed in the United States and numerous countries worldwide. Both vaccine formulations have shown excellent efficacy with minimal toxicity in active female population but numerous questions arise in vaccinating like cost effectiveness, lack of proven efficacy against other HPV strains, social acceptance of HPV vaccination and other ethical issues. The main objective of this study is to emphasis the advantages and disadvantages of the vaccination in India.**

**Keywords:** Cervix cancer - Gardasil - Cervarix - vaccine - HPV

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## Introduction

Cervical cancer is the second most common cause of cancer-related deaths in women worldwide (National cancer Institute, 2010). Cervical cancer is cancer that starts in the cervix, the lower part of the uterus that opens at the top of the vagina. Cervical cancer usually develops very slowly. It starts as a precancerous condition called dysplasia. Undetected precancerous changes can develop into cervical cancer and spread to the bladder, intestines, lungs, and liver. It can take years for precancerous changes to turn into cervical cancer (National Comprehensive Cancer Network, 2011). Patients with cervical cancer do not usually have problems until the cancer is advanced and has spread (Smith et al., 2010; Gauravi et al., 2011).

Cervical cancer is the most common cancer among Indian women and was estimated to have been responsible for 134,420 new cases and 72,825 deaths in the year 2008. India contributes to 25.4% and 26.5% of the global burden of cervical cancer cases and mortality, respectively. The age-standardized incidence rate and age-standardized mortality rate of cervical cancers are 27.0 and 15.2, respectively, among Indian women. Cervical cancer is responsible for 25.9% of all cancer cases and 23.3% of all cancer deaths among Indian women (Kawana et al., 2009).

Screening for cervical cancer is accomplished utilizing a Pap smear and pelvic exam (Ferenczy et al., 2001). While this technology is widely available and has reduced cervical cancer incidence in industrialized nations, it is not readily available in many third world countries like India in which cervical cancer incidence and mortality is high. Development of cervical cancer is associated with infection with high risk types of human papillomavirus (HPV) creating a unique opportunity to prevent or treat cervical cancer through anti-viral vaccination strategies (Winer et al., 2006; Tovar et al., 2008).

Cervical cancers are caused by HPV infections, with just two HPV types, 16 and 18, responsible for about 70 percent of all cases (Herrero et al., 2009; Gauravi et al., 2011). HPV also causes anal cancer, with about 85 percent of all cases caused by HPV-16. HPV types 16 and 18 have also been found to cause close to half of vaginal, vulvar, and penile cancers (Munoz et al., 2006; Noller et al., 2007).

The traditional cancer treatments consist of radiation therapy, chemotherapy, surgery and/or hormone therapy. They are rarely curative for disseminated cancers. On the other hand immunotherapy, especially vaccines, have become very attractive, because of the possibility of an effective treatment, with the potential to last of a lifetime.

Currently two vaccines are available for cervical cancer they are Gardasil and Cervarix.

## Vaccination

HPV is largely asymptomatic, making it difficult to recognize and detect among the general population, which will limit any behaviour modification. Vaccinations may thus provide a solution for prevention. Two different vaccines that have been developed to prevent infection from HPV 16 and 18.

Gardasil has been developed that protects against the two high-risk HPV types (types 16 and 18), which cause 70% of cervical cancers in women and 90% of all HPV-related cancers in men. It also protects against two low-risk HPV types (types 6 and 11), which cause 90% of genital

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warts (Kawana et al., 2009).

Cervarix is available, which protects against the same two high-risk HPV types (types 16 and 18). It does not protect against low-risk HPV types which cause genital warts (Kari et al., 2008). Some doctors may recommend this vaccine rather than Gardasil (Department Of Health And Human Services, 2011).

## HPV Vaccination

In many women the vaccine successfully prevents pre-cancerous changes which may develop into cervical cancer. The scientific trials which looked at the vaccine that targets four HPV strains showed that the risk of pre-cancerous changes caused by HPV 16 and 18 is generally low. It was only 2-3% in women who had not been vaccinated, compared to 1-2% in those who had. In other words, the vaccine prevented the development of pre-cancerous changes in about 1 out of every 100 women during the trial. It is assumed that the vaccine works even better in girls and women who have not been infected with HPV – but researchers disagree about the estimates of possible benefit (Sankaranarayanan et al., 2006). The vaccine was also shown to reduce the frequency of genital warts from 4% in women who were not vaccinated to 1% in those who were (1 in every 100 women).

According to current knowledge, the protective effect of the vaccine lasts at least five years. It is not yet known whether a booster vaccination is needed after this. The vaccine cannot be used to treat HPV infections or genital warts once women have them.

Because it is not yet known how well the vaccine works in the long term, and because cervical cancer usually develops very slowly, at the moment it is unclear whether the HPV vaccine really lowers the number of people who get cervical cancer. Being so new, there is also no evidence to show whether it reduces the number of women who die from this disease either.

One benefit of having the vaccine is that it can prevent pre-cancerous changes from developing. The diagnosis and treatment of these changes can be very stressful for women. Every year, thousands of women have surgery to remove pre-cancerous tissue – it is not known exactly how many women do though (Fact sheet Pubmed, 2010).

## Administration of HPV Vaccine

The vaccine is injected into the muscles of the upper arm. It does not contain any genetic material (DNA) of the viruses. Instead, genetically engineered virus-like particles are used. These have the same outer protein coat as the viruses do, but do not carry any genetic information. The particles activate the body's immune system and trigger the production of protective antibodies without causing an infection. Depending on the vaccine, the second dose is given one or two months after the first dose, and the third dose is given six months after the first dose (Singh et al., 2005).

## Benefits of HPV Vaccination

Vaccines helps to protect girls and young women ages 9-26 against 70% of vaginal cancer cases and up to 50% of vulvar cancer cases (Satija, 2010). Vaccination was 90% effective in reducing the risk of persistent HPV16/18 infections. 65 million doses of Gardasil have been given safely, in over 100 countries around the world (US Food and Drug Administration, 2010).

Both vaccines have been shown to prevent cervical precancer in women.

Both vaccines are very safe.

Both vaccines are made with a very small part (in this case, the protein outer coat) of the human papillomavirus (HPV) that cannot cause infection.

## HPV Vaccine Controversy

Gardasil® (Merck and Co., Inc., Whitehouse Station, NJ) is the first vaccine approved by US Food and Drug Administration (FDA) in June 2006, which provides 100% protection against HPV 16 and 18, and protects

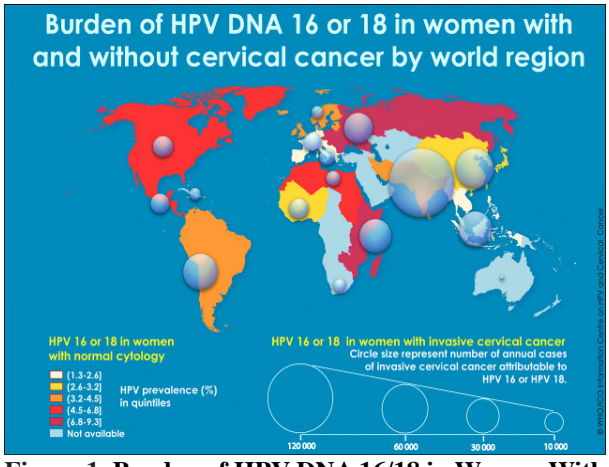


**Figure 1. Burden of HPV DNA 16/18 in Women With and Without Cervical Cancer by World Region.** Source: WHO/IC O Information Centre on Human Papilloma Virus (HPV) and Cervical Cancer (b),http://www.who.int/hpvcentre/statistics/statistics_map_ICO.pdf

**Table 1. Crude and Age-adjusted Incidence Rates per 100,000 Population for Cervical Cancer in 12 PBCRs in India**

| | | Crude Incidence Rate | Age-Adjusted Incidence Rate |
|---|---|---|---|
| PBRC: | Bangalore | 18.8 | 21.7 |
| | Barshi | 42.7 | 22.4 |
| | Bhopal | 22.2 | 24.5 |
| | Chennai | 24.4 | 30.6 |
| | Delhi | 16.3 | 22.7 |
| | Mumbai | 14.6 | 18.0 |
| | Ahmedabad | 16.2 | 13.4 |
| | Karunagappally | 19.2 | 15.0 |
| | Kolkata | 17.5 | 19.9 |
| | Nagpur | 19.1 | 23.2 |
| | Pune | 20.5 | 22.5 |
| | Thiruvanathapuram | 13.1 | 10.9 |

*National Cancer Registry Programme and World Health Organisation, Atlas of Cancer in India

against HPV type 6 and 11. Cervarix® (GlaxoSmithKline, Research Triangle Park, NC) against HPV type 16 and 18 was first licensed in 2007 and was initially approved only in Europe. In October 2009, the FDA approved its use in the United States. Studies show that Cervarix is 93% effective in preventing cervical precancerous changes. Both vaccines require a series of 3 0.5-mL intramuscular injections. The vaccines form virus-like particles, are noninfectious, and are designed for prophylaxis only. Western nations have been tackling questions that address who requires the vaccine and at what age girls should receive it. The US Advisory Committee on Immunization Practices recommends that girls and women between the ages of 9 and 26 years should receive the quadrivalent vaccine. The WHO position paper on the HPV vaccine recommends that it should be a part of national immunization programs. WHO recommends the vaccine be given between the ages of 9 and 13 years, prior to a girl's first coitus. However, they acknowledged nationwide administration of HPV vaccine would only be cost effective in countries that have high gross domestic products (World Health Organization, 2009).

In developing countries like India where HPV infection is high [WHO/ICO Information Centre on Human Papilloma Virus and Cervical Cancer (a)], introducing a national HPV vaccination programme may reduce the incidence of cervical cancer. However, the primary obstacle to this is financial, as the vaccines are expensive in relative terms. Public sector spending in health is very low in India (India spent 3.6% of its GDP on health in 2007) (WHO, 2009), making it difficult for the government to independently take on the task of introducing the vaccine in the national immunization programme, without external support. Thus although the vaccine is available for personal use in India, it has not been implemented at the population level. However, with an annual per capita income of 38,084 INR (for the year 2008-09) ,the average Indian cannot afford to pay for the HPV vaccine which costs 12,000. INR at 2009 prices for 3 doses It is yet unclear how many women in India have taken this route although one study demonstrated that parents of adolescent girls in Mysore have a positive attitude towards the vaccine. Nevertheless, the vaccine is still surrounded by controversy in the country. Although the vaccination can prevent cervical cancer to some extent, it cannot completely protect and fight against the cancer (Herrero, 2009).

Vaccines cannot substitute screening and treatment of cervical precancer. There are several challenges for the vaccine to be successfully used to control this largely preventable disease, including endorsement by governments and policy makers, affordable prices, education at all levels, overcoming barriers to vaccination, etc. Currently ongoing research is focused on the development of HPV vaccines that will offer protection against a broader range of HPV types and in the development of therapeutic vaccines, which seek to elicit immune responses against established HPV infections and HPV-induced cancers (Kawana et al., 2010).

Tiered pricing with the help of WHO, international organizations, and other funding sources might make this possible. However, the HPV vaccine is not an immediate panacea. Even if the vaccine were affordable and widely available in resource-poor settings, the rate of cervical cancer would not decline for decades as a result of the latency phase between infection and cancer (Schiffman et al., 2009).

## Conclusion

Although many effective screening methods like Pap smear are available to detect cervical cancer in early stages It is evident that regular Papanicolaou tests are impractical. Unless funding becomes available to bear the cost of the HPV vaccine, it will not realistically be available to women in developing nations. Although Cervarix and Gardasil protect against infection with HPV 16 and 18, these vaccines do not protect against HPV types found in approximately 30% of cervical cancers. women who have been vaccinated need to continue to have pap smears. Compounds like Carrageenan, extracted from seaweed has microbicide which prevent form genital HPV infection are in clinical trials. NIH is also supporting to make cervical cancer prevention, screening and treatment more affordable in developing nations like India to reduce cervical cancer incidence and mortality. In spite of all these efforts more research is needed in the Indian context, to evaluate interventions for cervical cancer and assess their applicability, success, scalability and sustainability within the constraints of the Indian health care system.

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